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EXAMINER
FOSTER, CHRISTINE E

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/711,517	ABBOTT ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-41* is/are pending in the application.

4a) Of the above claim(s) *24-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13-23* is/are rejected.

7)☒ Claim(s) *14 and 23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/30/06, 2/23/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendments to claims 1, 3, 7, 9, 11, 13, 14, 18 and 23 in the amendment filed 5/19/06 are acknowledged and have been entered. Claim 12 has been canceled. Claims 1-11 and 13-41 are pending in the application, with claims 24-41 currently withdrawn.

Objections/Rejections Withdrawn

2. The objection to the specification regarding use of trademarks is withdrawn in response to Applicant's amendments.

3. The objections to claims 3, 9, 11 and 13 are withdrawn in response to Applicant's amendments.

4. The rejection of claim 18 under 35 USC 112, 1st paragraph (written description) is withdrawn in response to Applicant's arguments (p. 10-11).

5. The rejections under 35 USC 112, 2nd paragraph not reiterated below have been withdrawn.

Sequence Compliance

6. The specification is objected to for the following reasons.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). A computer readable form (CRF) of the sequence listing was submitted on 12/21/05. However, the

CRF could not be processed by the Scientific and Technical Information Center (STIC) for the reason(s) set forth below.

When using the identifier "Artificial" for the numeric identifier <213> the source of the genetic material must be provided in a feature field. In SEQ ID NO:1 the source of the material was correctly provided as "synthetic", but for SEQ ID NO:2 there was no source listed in either feature.

Applicant's time to comply with the sequence rules is set forth on the attached Office Action Summary (Form PTOL-326). Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period.

Information Disclosure Statement

7. Applicant's Information Disclosure Statements filed 1/30/06 and 2/23/06 have been received and entered into the application. The references therein have been considered by the examiner as indicated on the attached form PTO-1449.

Citation S7 on the IDS of 2/23/06 has been lined through because it is a Japanese language document.

Citations 3 and 18 on the IDS of 1/30/06 have been lined through because the references were previously cited by the Examiner and are already of record. Similarly, US Patents 6,852,285 and 6,096,386 were previously cited by the Examiner.

Citation 31 of the IDS of 1/30/06 has been lined through because the reference also appears as Citation S8 on the IDS of 2/23/06.

Drawings

8. The drawings are objected to because in Figures 4.2 and 6.2 portions of the text are still unreadable (see the drawings filed 5/19/06). The replacement drawings submitted also did not include all of the figures.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. **Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended.** The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Objections

9. Claim 14 is objected to because it depends from a rejected claim (claim 12). For the purposes of examination claim 14 has been assumed to depend from claim 1.

10. Claim 23 is objected to because it recites that "orientation of the liquid crystal is detected optically or electrically", but fails to clearly convey how this detection step is related to the detection method of claim 1. Detecting the orientation of the liquid crystal would seem to relate back to the detection of the ligand in claim 1, yet the claim does not clearly recite that detecting the orientation of the liquid crystal results in detection of the ligand.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claim 13 as amended now recites that “each receptor” “independently has specificity for one ligand” and that the liquid crystal is capable of detecting the presence of “more than one ligand”. It is unclear whether each receptor is specific for different types of ligands or for the

same one ligand (see rejection under 112, 2nd paragraph below). It is also unclear what is meant by each receptor "independently" having specificity.

However, the claim encompasses a scenario in which multiple, different receptors all having specificity for the same ligand are used, which represents a departure from the specification and claims as originally filed.

Applicant points to the specification at [0181], in which different antibodies were arrayed in order to detect phosphorylated proteins (see Applicant's response, p. 16-17). There is no specific disclosure in this section that the different antibodies "independently" have specificity for the same ligand. Furthermore, Applicant has not established that the specific antibodies referred to are necessarily and always specific for the same one ligand, and that such a feature would have been recognized as such by those skilled in the art.

In addition, the specification does not provide any generic teaching of a method wherein each of a plurality of receptors "independently" have specificity for one ligand, or of a method with different receptors all having specificity for the same one ligand.

Applicant's reliance on a single or limited species (the specific antibodies of [0181], which were used to detect the phosphorylated protein EGFR) does not provide sufficient direction and guidance to the features currently claimed. This specific example pointed by Applicant relates to a particular set of reagents, while claim 13 is not limited in scope to such reagents. The disclosure of a single species in which multiple, different receptors may have specificity for the same ligand fails to support the genus that is now claimed. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1-11 and 13-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

15. Claim 1 recites the limitation "the receptor" in lines 6 and 8. There is insufficient antecedent basis for this limitation in the claims since line 2 refers to a "plurality of receptors"; it is unclear which of the plurality of receptors is being referred to.

16. Claim 1 recites the limitation "the detection surface having a detection substrate and a liquid crystal" in part (c). There is insufficient antecedent basis for this limitation since the previous reference to a "detection surface" in part (b) does not state that the surface has a substrate and a liquid crystal.

17. Claim 1 recites a detection surface "having a detection substrate and a liquid crystal" in part (c). The claim is indefinite because this would imply that the detection surface comprises a liquid crystal at the time that it is contacted with the affinity substrate, yet the specification discloses that "[t]ypically, the liquid crystal is placed on the detection surface after it has been contacted with the affinity substrate" (p. 15).

18. Claim 3 recites a Markush group terminated with "or a fragment thereof". Because of the grammatical structure of the sentence it is unclear whether "a fragment thereof" refers to fragments of only the last member of the Markush group (a herbicide) or to fragments all of the Markush group members.

19. Claim 6 recites a method wherein PDMS is "peptide-terminated". It is unclear what is meant by "peptide-terminated". Is the peptide the receptor in this instance? Is the peptide attached to PDMS?

20. Claims 7 and 9 recite a method wherein a species is "capable of binding to" a phosphorylated peptide (claim 7) or a protein (claim 9). The claims are indefinite because it would appear that the bound species would correspond to the "ligands" recited in claim 1, but this is not explicitly stated.

21. Claim 7 is also rejected as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the specification discloses that peptide-terminated PDMS stamps are used to detect phosphorylated peptides by contacting the peptide-terminated stamp with phosphospecific antibodies (see paragraph 197). As there is no disclosure of any other means by which peptide-terminated PDMS may be capable of detecting phosphorylated protein, the phosphospecific antibodies are an essential element that is omitted from the claims.

22. Claim 8 recites "antibody-terminated" PDMS. It is unclear how PDMS is terminated by an antibody, as discussed above.

23. Claims 13-14 recite the limitation "the array". There is insufficient antecedent basis for this limitation in the claims.

24. Claim 13 recites that each receptor "independently has specificity for one ligand" and that the liquid crystal is capable of detecting the presence of "more than one ligand". It is unclear whether each receptor is specific for different types of ligands or for the same one ligand. If each

receptor is specific for the same ligand, it is unclear how the liquid crystal would be used to detect more than one type of ligand.

25. It is also unclear what relationship the "one ligand" and the "more than one ligand" that are recited in claim 13 have with the "ligand" of claim 1. Is the "one ligand" recited the same as that of claim 1?

26. In claim 13 it is also unclear what is meant by the adjective "**independently**" in this context--in what sense do the receptors "independently" have specificity for ligand(s)? The use of this terminology in reference to receptor specificity is not defined in the specification, such that one skilled in the art would not be reasonably apprised of the scope of the claimed invention.

27. Claim 18 recites a partially curved affinity substrate. The term "partially curved affinity substrate" is indefinite because the specification discloses that "The method comprises the steps of: (a) contacting the ligand to a first surface, wherein the ligand is at least in part attached to the first surface; (b) contacting the ligand-decorated first surface to a second surface, wherein the ligand is at least in part attached to the second surface, such that at least a portion of the first surface is partially curved." It would therefore seem from this description that at least a portion of the affinity substrate is partially curved as a result of steps (a) and (b). However, the claim language suggests that the affinity substrate is inherently curved. It is also unclear whether "partially" refers to a part of the affinity substrate or to partial curvature.

Claim Rejections - 35 USC § 103

28. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

29. Claims 1-5, 8-11, 13, 15-20 and 22-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. ("Affinity capture of proteins from solution and their dissociation by contact printing" (2001) *Nature Biotechnology* **19**:866-869) in view of Abbott et al. (US Patent No. 6,852,285 B2, previously published January 10, 2002 as US 2002/0004216).

Bernard et al. teach a method for detecting a ligand comprising (a) contacting a sample having a ligand (e.g., ^{125}I-IgG in PBS containing 10% fetal calf serum) with an affinity substrate (polydimethylsiloxane (PDMS) stamp), wherein the affinity substrate comprises a plurality of receptors capable of specifically binding the ligand (anti-mouse IgG) (see Figures 1-2 p. 866, in particular the abstract, left column, and the first paragraph of "Results and Discussion"). There are a "plurality" of receptors covalently immobilized on the affinity substrate as depicted in Figure 1. Bernard et al. further teach (b) contacting the PDMS stamp with a detection surface (glass or polystyrene), wherein at least a portion of the ligand which is bound to the receptor is transferred to the detection surface (see in particular p. 866, left column, second paragraph, and the first paragraph of "Results and Discussion"; p. 869, "Affinity stamping").

Bernard et al. fail to teach that the detection surface further comprises a liquid crystal, or that the presence of the ligand is detected with the liquid crystal.

Abbott et al. teach a method for detecting a ligand comprising contacting a ligand with a detection surface ("substrate"), wherein at least a portion of the ligand is transferred to the detection surface, and detecting the presence of the ligand on the detection surface ("substrate), wherein the detection surface comprises a liquid crystal (see column 5, lines 29-35 and line 62 to column 6, line 1-5; column 13, lines 15-21; column 13, lines 7-35; column 14, lines 20-47). In particular, Abbott et al. teach liquid crystal devices comprising one or more substrates for

detection of ligand ("analyte"), wherein the ligand is contacted with a substrate that contains a receptor ("recognition moiety") for the analyte as well as a liquid crystal (mesogens), which undergo a detectable switch in orientation upon interaction of the ligand and receptor, allowing for the ligand to be detected. The use of liquid crystals in the detection surface of Abbott et al. obviates the need for prelabeling of ligand, such as with a radiolabel or a fluorescent moiety (see column 5, lines 7-12).

Therefore, it would have been obvious to one of ordinary skill in the art to employ the detection surface comprising a liquid crystal of Abbott et al. in the method for detecting a ligand of Bernard et al. in order to detect the presence of the ligand because Abbott et al. teach that liquid crystal detection surfaces do not require labeling of the ligand (as was performed in Bernard et al.). One would have reasonable expectation of success in affinity stamping the surface of Abbott et al. according to the method of Bernard et al. because the surface of Abbott et al. is compatible with stamping by microcontact printing (see column 17, lines 5-22).

With regard to claim 2, Bernard et al. teach washing the affinity substrate after the inking step (a) above (p. 869, "Affinity stamping").

With regard to claims 4-5, Bernard et al. teach affinity substrates consisting of PDMS as an inert elastomer (p. 866, left column, paragraph 3).

With regard to claims 8-9, the PDMS affinity substrates of Bernard et al. would seem to be "antibody-terminated" because the antibodies are attached to the ends of PDMS stamps (Figure 1). The antibodies are capable of binding to a protein (^{125}I-IgG). Bernard et al. teach the use of antibodies in this context as capturing molecules (e.g., see p. 866, first two paragraphs of "Results and Discussion").

With regard to claim 10, Bernard et al. teach that the antibodies, protein A, and streptavidin were applied to the affinity stamps via the cross-linker BS3 (p. 869, "Derivatization of stamps").

With regard to claim 11, while not specifically recited by Bernard et al., the amount of ligand present in the sample was inherently quantified because Bernard et al. teach the concentrations of the ligands TRITC-labeled rabbit IgG and biotinylated alkaline phosphatase in the samples (see p 869, "Affinity Stamping).

With regard to claim 13, Bernard et al. (as noted above) teach that the PDMS stamp may be patterned with arrayed capturing sites with various types of receptors for screening several analytes in a parallel manner (p. 868, right column). One skilled in the art would immediately envisage that "various types of receptors" would mean receptors that have specificities for different ligands. It is also noted that Bernard et al. teach a stamp with distinct locations in the form of a surface relief of parallel lines spaced evenly apart (p. 868, left column, the third full paragraph and Figure 4D in particular). It would also seem that the teeth of the PDMS stamps comprise distinct locations on which arrays of receptors are located (Figure 2A). Since there are multiple receptors, the array is capable of binding to and therefore detecting multiple ligands (see Applicant's response at p. 17, the first paragraph). This anticipates the claimed limitation since the claim does not require *different* types of receptors and *different* types of ligands.

Also with regard to claim 13, Abbott et al. teaches that the liquid crystal detection surface is capable of detecting the presence of more than one ligand, such as by using combinatorial library of compounds (see column 37, line 62 to column 38, line 22).

With regard to claims 15-17, Abbott et al. further teach that the detection surface may comprise self-assembled monolayers in order to anchor the liquid crystal mesogenic layer, where the self-assembled monolayers may be formed from alkanethiols or organosulfur compounds and may comprise amines through functionalization (the abstract; column 19, lines 32-42 and column 20, lines 1-7). Abbott et al. teach that the detection surface may be treated with 1-aminododecanoic acid to make the surface surface-active (column 25, lines 30-35). With regard to claim 19, Abbott et al. teach that use of certain self-assembled monolayers enables homeotropically anchoring of mesogens (column 19, lines 36-40 and column 12, lines 62-64 in particular).

With regard to claim 18, the specification discloses that "The method comprises the steps of: (a) contacting the ligand to a first surface, wherein the ligand is at least in part attached to the first surface; (b) contacting the ligand-decorated first surface to a second surface, wherein the ligand is at least in part attached to the second surface, *such that at least a portion of the first surface is partially curved"* (paragraph 28, emphasis added). Because Bernard et al. teach steps (a) and (b) as recited in the passage above, it would seem that the affinity substrate of Bernard et al. meets this limitation since the specification discloses no specific structural limitations associated with a partially curved surface, but rather indicates that the partial curvature is merely a result or conclusion of the steps above.

With regard to claims 20 and 22, the liquid crystal mesogens of Abbott et al. may be thermotropic or lyotropic and may be nematic, chiral nematic, smectic, frustrated liquid crystals, or discotic liquid crystals (column 30, line 33 to column 32, line 29), and a preferred liquid crystal is 4-cyano-4'-pentylbiphenyl (5CB) (column 37, lines 57-61).

With regard to claim 23, Abbott et al. teach that the detection surface allows for optical detection of orientation of the liquid crystal (mesogens) (the abstract and column 5, lines 15-26), and further teaches that optical output allows for ease of detection (column 5, lines 15-19).

30. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. in view of Abbott et al. as applied to claims 1 and 5 above, and further in view of Houseman et al. ("Maleimide-Functionalized Self-Assembled Monolayers for the Preparation of Peptide and Carbohydrate Biochips" (2003) *Langmuir* **19**:1522-1531, Published on Web 11/13/2002).

Bernard et al. and Abbott et al. are as discussed above. Bernard et al. teaches a method in which the PDMS stamp is antibody-terminated, but fails to teach a method wherein PDMS is terminated with a peptide.

Houseman et al. teach peptides that may be immobilized to substrates and tested for their ability to serve as substrates for phosphorylation by a kinase (p. 1527, "Characterization of Kinase Activity"). Peptides that have been successfully phosphorylated are then detected by binding to phosphotyrosine-specific antibody.

It would have been obvious to employ peptides immobilized to substrates and react them with kinases, as taught by Houseman et al., as the capturing molecules (receptors) in the method of Bernard et al. in order to characterize kinase activity and establish whether the peptides are substrates of kinases. Peptides that are phosphorylated would then be capable of interacting with phosphotyrosine-specific antibody, as taught by Houseman, such that the phosphorylated peptide-terminated PDMS stamp could be inked with the phosphotyrosine-specific antibody (ligand) according to the method of Bernard et al. Detection of the phosphotyrosine-specific

antibody stamped onto the surface of Abbott et al. could therefore be detected to detect the phosphorylated peptide. One would have a reasonable expectation of success because Bernard et al. teach that "[a]ny type of ligand-analyte interaction may be exploited" (p. 868, right column).

31. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. in view of Abbott et al. as applied to claim 1 above, and further in view of Tang et al. (US Patent No. 5,886,195).

As discussed above, Bernard et al. teaches PDMS stamps that comprise a plurality of IgG receptors, and also teach stamps patterned with various types of receptors. The liquid crystal detection surface of Abbott et al. is capable of detecting the presence of more than one ligand. However, the references fail to specifically teach a method wherein the receptors are capable of detecting the presence of protein phosphorylation in EGFR residues.

Tang et al. teach anti-phosphotyrosine antibodies, which may be used to measure autophosphorylation of EGFR and thereby an increase in EGF activity (column 6, lines 53-65).

Therefore, it would have been obvious to one of ordinary skill in the art to employ anti-phosphotyrosine antibodies as the capturing molecules on the PDMS stamp in the method for detecting a ligand of Bernard et al. and Abbott et al. in order to measure autophosphorylation of EGFR. One would have reasonable expectation of success because Bernard et al. teach the use of antibodies as capture molecules on PDMS stamps.

32. Claim 21 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bernard et al. in view of Abbott et al. as applied to claim 1 above, and further in view of Tarlov et al. ("UV

Photopatterning of Alkanethiolate Monolayers Self-Assembled on Gold and Silver" (1993) *J. Am. Chem. SOC.* 115, 5305-5306).

Bernard et al. and Abbott et al. are as discussed above, which fail to treat a method wherein a liquid crystal is pretreated by illumination with UV light.

Tarlov et al. teaches UV photopatterning of self-assembled monolayers on gold and silver (p. 5305, in particular the paragraph bridging the left and right columns).

It would have been obvious to pretreat the liquid crystal detection surface of Abbott et al. with UV light, as taught by Tarlov et al., in order to pattern the surface because Abbott et al. teach that the surface may be patterned by various techniques in order to produce patterns such as adjacent wells (see column 13, lines 5-64). One would have a reasonable expectation of success in employing the UV patterning method of Tarlov because Tarlov teaches patterning of alkanethiol monolayers on gold, which are embodiments also taught by Abbott et al.

Response to Arguments

33. Applicant's arguments filed 5/19/06 have been fully considered.

34. With respect to the rejection of claim 1 under 112, 2nd paragraph regarding the detection surface and liquid crystal (see the previous Office action at item 6), Applicant's arguments and amendments have been fully considered but they are not persuasive. The current claim language appears to suggest that the detection surface is made up of a detection substrate and a liquid crystal, such that at the time that the detection surface is contacted with the affinity substrate, the liquid crystal is already present. This would exclude the scenario disclosed in the specification, which states that "[t]ypically, the liquid crystal is placed on the detection surface *after* it has been

contacted with the affinity substrate" (p. 15, emphasis added). Thus it remains unclear whether the liquid crystal is present on the detection surface when it is contacted with the affinity substrate.

35. With respect to the rejections of claims 6-9 under 112, 2nd paragraph for recitation of "peptide-terminated" and "capable of detecting" (now amended as "capable of binding"), Applicant's arguments (p. 15-16) have been fully considered but they are not persuasive. The claims appear to recite limitations relating to the nature of the receptors and/or the ligands that are detected by the method, but this is not clearly stated, such that it is unclear how the additional limitations relate to the method of detecting of claim 1. For example, claim 6 recites that the affinity substrate is peptide-terminated, but does not recite that the peptide is acting as the receptor in this case.

36. With respect to the rejection of claim 7 under 112, 2nd paragraph for missing essential element, Applicant submits that no essential elements are missing from the claims, to which the Examiner disagrees as the missing element of a phosphospecific antibody is still not recited in the claim.

37. With respect to the rejections of claims 12 (now cancelled) and 13 under 112, 2nd paragraph, Applicant's arguments have been fully considered but are moot in light of the new grounds of rejection set forth above.

38. With respect to the rejection of claim 18 under 112, 2nd paragraph for recitation of a "partially curved affinity substrate", Applicant argues that the term is clear and definite and points to the disclosure of a cylindrical stamp (Applicant's response, p. 10-11 and p. 18). This argument has been fully considered but is not persuasive. The claim does not recite a

"cylindrical" stamp, but rather a "partially curved affinity substrate". The specification passages referred to by Applicant do not mention a "partially curved affinity substrate". The only context in which a "partially curved affinity substrate" is disclosed (see above and the previous Office action at p. 17) does not relate to the use of cylindrical affinity stamps, but rather suggests that partially curved affinity substrates form during the performance of the claimed binding and detection method as a result of the contact between the affinity substrate and the detection surface. As such, the recitation of a "partially curved affinity substrate" is indefinite because it is unclear whether the partial curvature occurs during the method as a result of contacting the affinity and detection substrates, or alternatively whether the affinity substrate is partially curved at the outset (a cylindrical stamp). Thus, one skilled in the art reading the disclosure would not be reasonably apprised of the scope of the invention.

39. With respect to the rejections of claims 1-5, 8-11, 12 (now cancelled), 13, 15-20 and 22-23 under 35 USC 103(a) as being unpatentable over Bernard et al. in view of Abbott et al., Applicant argues that Bernard et al. does not enable one skilled in the art to make and use the claimed invention as amended, in that Bernard et al. does not enable or teach how to make arrays of proteins or "smart stamps" (Applicant's response, p. 19), to which the Examiner disagrees. The courts have stated that claims must be given their broadest reasonable interpretation consistent with the specification. See In re Morris, 127 F.3d 1048, 1054-55, 44 USPQ2d 1023, 1027-28 (Fed. Cir. 1997); In re Prater, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969); and In re Zletz, 893 F.2d 319, 321-22, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989) (see MPEP 2111). The amended claims do not require different types of receptors, only a plurality of

receptors. Bernard et al. teaches affinity substrates having a plurality of receptors, as depicted for example in Figure 1, thereby meeting the claimed limitation.

40. Applicant further argues that there is no motivation to combine the references in that a detection surface including a liquid crystal may not be considered as an obvious design choice, and notes that this is a synergistic combination that results in a very minute quantity of ligand to be detected (see Applicant's response at p. 19, the last four lines to p. 20, the first paragraph). This argument has been fully considered but is not persuasive. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

41. Applicant further argues that Bernard et al. is in the field of microcontact printing while Abbott et al. is in the field of molecular interaction visualization, and that there is no motivation to combine these references in non-analogous fields, to which the Examiner disagrees as both Bernard et al. and Abbott et al. are in the field of detection of molecular interaction.

42. Applicant also points to In re Lee and states that a determination of whether there is motivation to combine references must be based on objective evidence of record. In particular, Applicant argues that the Examiner relied on a conclusory statement instead of identifying a real motivation to combine the references (see Applicant's response, p. 20-21), to which the Examiner disagrees. The Examiner has not relied on any assertion of 'common knowledge and common sense' but has rather set forth a motivation to combine the references identified by the Abbott et al. reference, which teaches that liquid crystals allow for easily detectable and label-

free detection of molecular interactions, which is particularly pertinent to the method of detecting interactions of Bernard et al. (see above and the previous Office action at item 23).

43. With respect to the rejections of claims 6-7, 14, and 21 as being unpatentable over Bernard et al. in view of Abbott et al. and further in view of Houseman et al., Tang, or Tarlov et al., Applicant's response did not include any specific arguments relating to the claimed limitations.

Conclusion

44. No claims are allowed.

45. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached at (571) 272-0823. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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